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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KOLKER, DANIEL E	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 12/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/611,257	SNUTCH ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/13/03 and 6/27/03 and 9/15/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-6,14 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6,14, 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2, 4, 5, 6, 14, and 18 are pending in the instant application. Claims 3, 7 – 13, and 15 – 17 have been cancelled by Applicant in the paper filed September 15, 2004.

Amendments filed January 13, 2003, June 27, 2003, and September 15, 2004 have been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections and Rejections

Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and is withdrawn.

Claim Rejections - 35 USC § 112, Second Paragraph

Claim 6 was rejected under 35 U.S.C., second paragraph because it referred to the production of "functional calcium channels". Applicant's amendment of June 27, 2003 refers the examiner to page 1, lines 13 – 16 of the specification wherein a definition of a calcium channel s provided. This definition reads as follows:

> "The rapid entry of calcium into cells is mediated by a class of proteins called voltage-gated calcium channels. Calcium channels are a heterogeneous class of molecules that respond to depolarization by opening a calcium-selective pore through the plasma membrane."

This definition does not limit the definition of "functional calcium channels" to recombinantly expressed calcium channels. The following is a verbatim quotation of claim 6, from the amendment filed September 15, 2004:

> "A method to effect production of a functional calcium channel which method comprises culturing the cells of claim 4 or 5 under conditions wherein said functional calcium channels are produced."

Claim 6 is drawn to a method of producing "functional calcium channels". However, as written, this claim could be interpreted in several ways. First, it could be interpreted to mean culturing the cells of claim 4 or claim 5 in such a manner as to effect expression of the recombinant calcium channels encoded by the vector of claim 1. It could also be interpreted to mean a

method of culturing cells to stimulate the production of endogenous calcium channels. Claims 4, and 5, from which claim 6 depends, are sufficiently broad as to include, for example, a culture of primary neurons transiently transfected with the DNA of claim 1. Under the second interpretation of claim 6 listed above, it appears applicant is claiming a method of effecting production of endogenous calcium channels. This could include, for example, L-type calcium channels which were well-known in the art (see Hille, p. 104), and could be present on the surface of the mammalian cells of claim 5, as well as the recombinantly expressed T-type $\alpha 1$ subunits. Because claim 6 can reasonably be interpreted in these two ways, it is vague and indefinite. Applicant's arguments of June 27, 2003 have been fully considered but have not been found persuasive. The examiner's rejection of claim 6 under 35 U.S.C. § 112 has not been overcome. This rejection could be overcome by inserting the word "recombinant" before "functional" on the first line of claim 6.

Claim Rejections - 35 USC §§ 101 and 112

Claims 1, 2, 4, 5, 6, and 14 were rejected under 35 U.S.C. 101 for lacking utility. In order for utility to be established, an invention must have either a well-established or asserted utility. An asserted utility must be specific and substantial. See MPEP § 2107.01. In the remarks filed January 13, 2003, applicant states that utilities are provided on page 5, lines 9 – 19, and page 9, lines 11 - 28 of the specification. Below is a consideration of the utilities asserted by applicant, specifically whether they are specific and substantial.

1. The design of peptides to produce antibodies to assess the location and expression of the protein. This utility is credible. However, it is neither specific nor substantial. Any protein can serve as antigen for the production of antibodies directed against it. Furthermore, the utility is not substantial. Applicant is again directed to MPEP § 2107.01, which states:

> "On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":
> (A) Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved;
> (B) A method of treating an unspecified disease or condition;
> (C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility;"

The asserted utility clearly falls under the category of basic research and thus is not substantial.

2. The production of the proteins in cell lines to determine the properties of the channels containing the subunits of the invention. This asserted utility is credible. However it is neither specific nor substantial. Any polynucleotide that encodes a polypeptide can be produced in a cell line if appropriately expressed. Applicant provides ample guidance for expression of cloned DNA in cells, particularly on page 12 of the specification. However, this can be done with any cloned DNA. Furthermore, this utility is not substantial. Determining the properties of channels containing the subunits of the invention *is basic research* and thus falls under (A) as listed in the quotation of MPEP §2107.01 above.

3. The use of said cell lines to evaluate the effects of pharmaceuticals and/or toxic substances on calcium channels that incorporate the subunits of the invention. This asserted utility is credible. However it is neither specific nor substantial. Any recombinantly expressed protein could be used in an assay to determine the effects of unnamed compounds on itself. Furthermore, the evaluation of pharmaceuticals and/or toxins on channels is basic research. This concept is discussed in further detail in Hille, pp. 59 – 62. While the examiner does not doubt that this research may lead to important discoveries about the mechanisms, etiology, or treatment of the diseases listed on page 5 of the specification, such research is a starting point and the materials involved therein (e.g. polynucleotides and cell lines) do not constitute patentable discoveries simply in light of their potential role in such research.

In the remarks of January 13, 2003, applicant asserts that identification of pharmaceuticals useful in treating "the indicated disorders" would be useful. However, applicant has not disclosed a specific nexus between a disease and the polypeptide encoded by the polynucleotides of the present invention. Applicant has listed several diseases and conditions which "are associated with undesired calcium channel activity" (specification, p. 9, line 18). However, as stated in MPEP § 2107.01, assertions that a novel DNA is useful for

> "diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed. Contrast the situation where an applicant *discloses a specific biological activity and reasonably correlates that activity to a disease condition* [emphasis added]. Assertions falling within the latter category generally are sufficient to identify a specific utility for the invention. Assertions that fall in the former category are insufficient to define a specific utility for the inventions, especially if the assertion takes the form of a general statement that makes it clear that a "useful" invention may arise from what has been disclosed by the applicant. *Knapp v. Anderson*, 477 F.2d 588, 177 USPQ 688 (CCPA 1973)."

Although the example given by the MPEP above is drawn to an asserted utility for a DNA as a diagnostic marker, the same logic can be applied here. Applicant's asserted utility for the polypeptide encoded by the claimed polynucleotides is as a tool in the discovery of drugs to treat disorders when no nexus has been established between the claimed invention and a specific disease condition. Therefore, this is not a specific or substantial utility.

The remarks filed January 13, 2003 include arguments that drugs that modulate other T-type calcium channels are useful, therefore the T-type calcium channel of the present invention should also be considered useful. These arguments have been fully considered and not found persuasive. The guidelines for utility examination under 35 U.S.C. 101 as published in the Federal Register, Vol. 66, No. 4, pages 1092 – 1099 are particularly informative. The far-right column of page 1096 applies to the instant case:

> "...where a class of proteins is defined by common structural features, but evidence shows that the members of the class do not share a specific, substantial functional attribute or utility, despite having structural features in common, membership in the class may not impute a specific, substantial, and credible utility to a new member of the class."

In the instant case, simply identifying the novel polynucleotides as encoding a member of the T-type calcium channel family is not sufficient to impute a utility, especially since the family is diverse and its members have different biophysical properties, sensitivities to channel blockers, and modulation by exogenous molecules (Yunker, 2003; see especially p. 578, left-hand column).

Applicant's remarks of January 13, 2003 indicate that drugs can treat disorders associated with T-type calcium channels. While that may in fact be the case, it is not relevant to the question of whether or not the polynucleotides of the present invention have utility. The fact that the specification of U.S. patent 6,309,858 indicates that candidate compounds of undisclosed structure are useful in the treatment of pain does not serve as evidence that the polynucleotides encoding novel α1G subunits of the present invention are themselves useful. The nucleic acids of the instant invention would be useful if there was a nexus between a disease or disorder and the polypeptide encoded by said nucleic acids. However, neither the specification nor the prior art discloses a nexus between α1G subunits and any disease or physiological disorder.

The remarks of January 13, 2003 direct the examiner's attention to the standards for utility set forth by the Federal Circuit in *In re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995), as well

as the decision rendered by the court in *Burroguhs Wellcome v. Barr Laboratories, Inc.* 40 F3d 1223, 32 USPQ2d 1915 (Fed. Cir. 1994, cert. Denied, 115 S. Ct. 2553 (1995). Applicant particularly points out that the *Brana* court ruled that the point at which a candidate pharmaceutical compound becomes useful is well before it is administered to humans, and, citing *Nelson v. Bowler & Crossley*, 626 F2d 853, 206 USPQ 881, 883 (CCPA 1980), that the requirement for further in vitro testing does not itself abrogate utility of a compound. Applicant's arguments have been fully considered but not found persuasive.

The claimed invention and the issues in the instant application differ significantly from those in *In re Brana*. Brana et al. had filed an application directed to 5-nitrobenzo [de]isoquinoline-1,3-dione compounds for use as antitumor substances, which differed from several prior art compounds due to the presence of a nitro group at one position on the compound and an amino or other amino group at a different position. In the prior art Paull et al. had disclosed similar compounds that had antitumor activity, and one of the similar compounds from Paull et al. "NSC 308847" had been found to have excellent activity against two specific in vivo murine tumor models. In addition to comparing the effectiveness of the claimed compounds of Brana et al. with that of the antitumor compounds disclosed in Paull et al., the specification of Brana et al. illustrated the cytotoxicity of the structurally similar claimed compounds of Brana et al. against human tumor cells in vitro, and concluded that these tests "had a good action." Brana et al. also supplied a declaration by Dr. Keilhauer, in which his tests indicated that the compounds of Brana et al. were far more effective as antitumor agents than structurally related antitumor agents disclosed in Zee-Cheng et al. when tested against two specific types of human tomor cells, HEp and HCT-29. The Federal Circuit concluded that these tumor models represented a specific disease against which the claimed compounds were alleged to be useful, and that the prior art and the declaration of Dr. Keilhauer supported the conclusion that one skilled in the art would be convinced of the applicants' asserted utility, even if some of the compounds were later found not to possess anti-tumor activity in human trials.

The compounds of Brana et al. were asserted to be antitumor agents, which have a specific, substantial and immediately testable activity, which are useful against a specific disease condition. In contrast, in the instant case, Applicants have asserted that the nucleic acids can be used in assays to discover drugs or modulators that may be implicated in a wide spectrum of diseases of disorders such as epilepsy, sleep disorders, cariac hypertrophy, arrhythmia and hypertension. This is not a specific disease or disorder, but a wide variety of

diseases or disorders that have a variety of etiologies. The instant application teaches that the members of the protein family encoded by the polynucleotides are expressed broadly, but do not show where the claimed polynucleotides are expressed, nor provide evidence of their connection with any disease. Additionally, the application of Brana et al. had working examples, cytotoxicity studies against human tumor cells *in vitro*, and additional later substantiation by a declaration showing antitumor action against two human tumor cell lines. This is in contrast to the instant situation, in which there is no example linking the polynucleotides or encoded proteins to a disease state, only assertions as to activity based on membership in a family of proteins. The issue is not that further characterization might be required – the compounds of Brana et al. would require further human clinical trials in order to determine effectiveness in humans. However, the compounds of Brana et al. had a specific asserted utility and could immediately be tested by methods known to one of ordinary skill in the art. This is not the situation in the instant case, in which extensive further research would be required to determine if the polynucleotide and encoded protein of the instant invention were even correlated with any type of disease or disorder.

Applicants have also cited *Burroguhs Wellcome v. Barr Laboratories, Inc.* as being relevant, particularly because (1) there is no requirement that experimental proof of the ultimate desired utility be set forth in the specification and (2) results with an analogous material are supportive of results for a referent material even early on. Applicant's arguments have been fully considered but not found persuasive. The last sentence of p. 7 of the remarks filed January 13, 2003 implies that the claims which receive support from *Burroguhs Wellcome v. Barr Laboratories, Inc.* are drawn to methods of identifying compounds. Applicant is reminded that the claims under examination are drawn to DNAs, host cells, and methods to effect production of proteins. No claims are drawn to methods of screening for modulators of a calcium channel, thus the argument is not germane. Even if claims were directed to methods of screening, such a method would not have a specific and substantial utility, since there is no nexus between any disease or disorder and the α1G subunits of T-type calcium channels disclosed.

Applicants have also cited *In re Cortright* 49 USPQ 2d 1464 (Fed. Cir. 1999) as providing relevant guidance for the establishment of utility. The Cortright decision is not relevant to the instant application. The claims in Cortright had been rejected under § 101, but that rejection was overturned by the court, which reasoned that the PTO must provide evidence

that one of ordinary skill in the art would doubt the asserted utility. In the instant case, Applicant points out, on p. 8 of the remarks filed January 13, 2003, that the Office has not provided evidence that compounds shown to modulate α1G T-type calcium channel activity would not be useful in treatment of diseases. Applicant is again reminded that the claims of the instant application are not drawn to those modulators (with undisclosed structures), or to the use of those in treating a broad list of diseases, from heart arrhythmias to mood disorders, but that the claims are drawn to polynucleotides, host cells, and methods to effect production of channels. No inherently implausible scientific principle has been asserted by Applicant; rather Applicant seems to be arguing that compounds yet to be discovered would have utility. The bar for utility set forth by § 101 must be met for the *claimed* invention, not a product which might be discovered later. Claims 1, 2, 4 – 6, and 14 remain rejected under 35 U.S.C. § 101 and § 112.

Claim 18 was not examined in the previous Office action. Claim 18 is drawn to polynucleotides encoding specific amino sequences which are α1G subunits. As stated above, no specific, substantial and credible utility for α1G has been disclosed by applicant. Therefore claim 18 is also rejected under 35 U.S.C. § 101. Further, claim 18 is rejected under 35 U.S.C. § 112. Since the invention of claim 18 lacks utility, a skilled artisan would not know how to use the invention.

Claim Rejections - 35 USC § 112

Claims 1,2, 4 – 6, and 14 were rejected under 35 U.S.C. 112, first paragraph, for failing to meet the written description requirement. The claims have been amended to recite specific SEQ ID NO:s. and those polynucleotides which encode polypeptides that are at least 99% identical on the amino acid level. The specification (p. 9 line 29 – p. 10 line 5) defines α1 subunits of T-type calcium channels. Page 8, lines 5 – 10 disclose that preferred embodiments include SEQ ID NO:24 and the sequences disclosed in Figure 6A – 6E (now referred to as SEQ ID NO:37), and those sequences at least 99% identical to them. Page 12, lines 2 – 5 indicate that the rat α1G subunit has amino acid sequence SEQ ID NO:24. The amendment filed January 13, 2003 indicates that the human α1G subunit has amino acid sequence SEQ ID NO:37. The physiological characteristics of the α1G subunit are established in Figures 1, 3, and 4. However, the claims are currently written include nucleic acid sequences that may encode functional α1G subunits. The written description rejection remains, but would be overcome if it

were further limited to recite functional limitations, such as "wherein the polypeptide transports calcium".

Priority Determination

35 U.S.C. § 120 states that:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

35 U.S.C. § 119(e) states that:

> An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 or § 119(e) from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention. Because the instant application does not meet the requirements of 35 U.S.C. § 112, first paragraph, for those reasons given above and it is a continuation-in-part of application Serial Number 09/346794, the prior application does not meet those requirements and, therefore, is unavailable under 35 U.S.C. § 120 or § 119(e). The effective priority date of the instant application is considered to be the filing date of this application, 7/6/2000, because the claimed invention is not supported by either a specific and substantial utility or a well-established utility.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4 - 6, and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Dubin et al., U.S. patent 6,358,706, filed October 26, 1999 and issued March 19, 2002. Claim 1 is drawn to an expression vector encoding a polypeptide at least 99% identical to SEQ ID NO:37. Dubin et al. teach a sequence 99.7% identical to SEQ ID NO:37; it is labeled as their SEQ ID NO:5. Furthermore, Dubin et al. teach operably linking said nucleic acid sequence to a vector to allow it to be expressed in cells (see specifically column 10, line 1 – 63), and explicitly claim this vector in claim 3 (column 59). Claim 4 is drawn to recombinant host cells that modified to contain the vector of claim 1. Dubin et al. teach the introduction of their vector into host cells (see column 11, first complete paragraph) and such cells are a part of their claim 5. Claim 5 from the instant application is drawn to mammalian cells. Dubin et al. specifically contemplate the use of mammalian cells (see column 11, line 1). Claim 6 is drawn to culturing the cells of claim 4 or 5 under conditions where functional calcium channels are expressed. Dubin et al. teach the culturing of cells under conditions to produce channels (column 28, Example 6) and explicitly claim this method (see their claim 5). Claim 14 is drawn to an isolated nucleic acid encoding a polypeptide at least 99% identical to SEQ ID NO:37. Dubin et al. specifically claim an isolated DNA molecule that encodes SEQ ID NO:5 (see claim 1, column 59). Therefore the teachings of Dubin et al. meet the limitations of claims 1, 4 - 6, and 14.

Conclusion

It is believed that all pertinent arguments have been addressed. No claim is allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PATENT EXAMINER